Complete Summary

GUIDELINE TITLE

Amantadine, oseltamivir and zanamivir for the treatment of influenza.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Amantadine, oseltamivir and zanamivir for the treatment of influenza. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Feb. 40 p. (Technology appraisal guidance; no. 168).

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: National Institute for Clinical Excellence (NICE). Guidance on the use of zanamivir, oseltamivir and amantadine for the treatment of influenza. London (UK): National Institute for Clinical Excellence (NICE); 2003 Feb. 30 p. (Technology appraisal guidance; no. 58).

The review date for this guideline is November 2013.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Influenza

Note: This guidance does not cover the circumstances of a pandemic, impending pandemic or a widespread epidemic of a new strain of influenza to which there is little or no community resistance.

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Family Practice
Geriatrics
Infectious Diseases
Internal Medicine
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of amantadine, oseltamivir, and zanamivirÂ for the treatment of influenza in children and adults

TARGET POPULATION

Children (1 to 14 years), adults (15 to 64 years) and the elderly (older than 65 years) with influenza who are considered to be either "otherwise healthy" or "at risk."

Note: For the purpose of this guidance, people 'at risk' are defined as those who have one or more of the following:

- Chronic respiratory disease (including asthma and chronic obstructive pulmonary disease)
- Chronic heart disease
- Chronic renal disease
- Chronic liver disease
- Chronic neurological conditions
- Diabetes mellitus

People who are aged 65 years or older and people who might be immunosuppressed are also defined as 'at-risk' for the purpose of this guidance.

INTERVENTIONS AND PRACTICES CONSIDERED

1. Zanamivir
2. Oseltamivir

Note: Amantadine was considered but not recommended for the treatment of influenza.

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Time to symptom alleviation
    - Time to return to normal activities
    - Time to alleviation of fever
    - Adverse effects (overall, serious, minor, and drug-related)
- Hospitalization
- Mortality
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this appraisal was prepared by the Centre for Reviews and Dissemination/Centre for Health Economics (CRD/CHE) Technology Assessment Group, University of York (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Search Strategy

Resources Searched

Studies were identified by searching the following databases: MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Pascal, Science Citation Index (SCI), BIOSIS, Latin American and Caribbean Health Sciences (LILACS), Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA) database. TOXLINE was also searched for studies with adverse event data. In addition, information on studies in progress, unpublished research and research reported in the grey literature was identified by searching Inside Conferences, Dissertation Abstracts, ClinicalTrials.gov, Current Controlled Trials, ClinicalStudyResults.org, Clinical Trial Results, World Health Organization International Clinical Trials Registry Platform (ICTRP), GlaxoSmithKline Clinical Trials Register, and Roche Clinical Trial Protocol Registry and Results Database. A methodological search filter was used to help

identify randomised controlled trials. The searches updated those undertaken for the original guidance and so were run from October 2001 to the present. Trial reports and additional data were provided by GlaxoSmithKline (zanamivir) and Roche (oseltamivir); no additional data were provided for amantadine (Alliance Pharmaceuticals).

Internet searches were carried out using the specialist search gateways Intute (www.intute.ac.uk) and MedlinePlus (http://www.nlm.nih.gov/medlineplus/) to identify relevant resources. Relevant websites were identified and searched included the British Lung Foundation, US National Institute of Allergy and Infectious Diseases, and US Centers for Disease Control and Prevention. Websites of regulatory agencies the US Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products (EMEA) were also searched. The full search strategies, dates and results of all searches are provided in Appendix 10.1 of the Assessment Report (see the "Availability of Companion Documents" field).

A supplementary search was undertaken to retrieve studies about drug resistance during the 2007/8 influenza season. This consisted of brief searches in MEDLINE and EMBASE, and the following disease surveillance websites: Health Protection Agency, World Health Organization Epidemic and Pandemic Alert and Response programme, and the European Centre for Disease Prevention and Control.

Inclusion and Exclusion Criteria

Two reviewers independently screened all titles and abstracts. Full paper manuscripts of any studies thought to be potentially relevant by either reviewer were obtained. The relevance of each study was assessed by two independent reviewers according to the criteria stated below. Any discrepancies were resolved by consensus, or where consensus could not be reached, a third reviewer was consulted. Non-English language papers were screened by one reviewer with a native speaker. Details of included studies are provided in Appendix 10.2 and a list of excluded studies and the reasons for their exclusion in Appendix 10.3 of the Assessment Report (see the "Availability of Companion Documents" field). For studies retrieved only as an abstract, authors were contacted to request additional information. Where additional information was not obtained, abstracts were included only if sufficient outcome data were available. Studies written in any language were included.

Study Designs

Only randomised controlled trials were included in the review of clinical effectiveness.

Interventions and Comparators

Studies of treatment with antiviral drugs compared to each other, to placebo, or to best symptomatic care were included. Only licensed antiviral doses and durations of use were included (refer to Appendix 4 of the Assessment Report [see the "Availability of Companion Documents" field]). Studies of prophylaxis were excluded, as were studies of intravenous and nebulised zanamivir as these are not licensed modes of administration.

Population

Studies of adults and/or children (in the age ranges indicated by the relevant licenses) who presented with symptoms typical of influenza were included, whether influenza was reported as circulating in the community or not. Studies reporting the efficacy of treatments during a pandemic, or a widespread epidemic of a new strain of influenza, were excluded as these situations are not covered by the new guidance. Studies of healthy volunteers with experimentally-induced influenza were also excluded.

Outcomes

The outcome measures were: time to alleviation of symptoms (composite of five or more symptoms); time to return to normal activity (encompassing varying definitions: able to perform usual daily activities, return to work or school, return to normal health and return to feeling as before illness); time to alleviation of fever; adverse events (overall, serious, minor and drug-related); and the incidence of influenza-related complications (overall, serious, antibiotic use, pneumonia, bronchitis and otitis media in children), hospitalisation and mortality. The numbers still with symptoms at final follow-up were extracted or calculated where possible.

Cost-Effectiveness

Search Strategy

Searches for economic evaluations were undertaken in the databases listed above for clinical effectiveness, replacing the randomised controlled trials search filter with an economic/cost methodological search filter. In addition, searches of National Health Service Economic Evaluation Database (NHS EED) and Health Economic Evaluation Database (HEED) were carried out, alongside a search of the Economics Working Papers archive (IDEAS). Searches for health-related quality of life studies were also undertaken.

A broad range of studies were considered for inclusion in the assessment of cost effectiveness, including economic evaluations conducted alongside trials, modelling studies and analyses of administrative databases. Only full economic evaluations that compared two or more options and considered both costs and consequences (including cost-effectiveness, cost-utility and cost-benefit analyses) were included.

Two reviewers independently assessed all obtained titles and abstracts for inclusion based on the search strategies reported in the Clinical Effectiveness section above and Appendix 10.1 of the Assessment Report (see the "Availability of Companion Documents" field). Any discrepancies were resolved by discussion and consultation with a third reviewer. All studies meeting the inclusion criteria were summarised and used as the basis for identifying major structural issues, assumptions and key drivers of cost-effectiveness. Due to the large number of individual studies identified, only the most relevant studies from the perspective of the NHS were then considered in more detail.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

A total of 29 randomized controlled trials (RCTs) were included for evaluation.

Cost Effectiveness

- Twenty one studies met the inclusion criteria.
- Economic models were provided by the manufacturer of oseltamivir and the Assessment Group.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by the Centre for Reviews and Dissemination/Centre for Health Economics (CRD/CHE) Technology Assessment Group, University of York (see the "Availability of Companion Documents" field.)

Data Extraction Strategy

Data relating to both study content and quality were extracted by one reviewer, using a standardised data extraction form, and checked by a second reviewer. Discrepancies were resolved by discussion, with involvement of a third reviewer when necessary. Non-English language studies were extracted by one reviewer with a native speaker. Attempts were made to contact authors and pharmaceutical companies for missing data. Additional data were provided by the manufacturers, GlaxoSmithKline (zanamivir) and Roche (oseltamivir). There was no company submission for amantadine (Alliance Pharmaceuticals). Data from multiple publications of the same study were extracted and reported as a single study unless there was no overlap in the outcomes reported. Where overlap did occur, results from the largest population were extracted. Extraction included data on: study characteristics (e.g., study ID, author, year, location, duration of follow

up, time from onset of symptoms to initiation of treatment, whether the study was reported as being conducted while influenza was circulating in community), patient characteristics (e.g., age, gender, number of participants and withdrawals, subgroups reported), interventions (dose and frequency of administration), comparators (placebo, symptomatic relief, or active comparator), study quality, and reported outcomes as specified in "Description of Methods Used to Collect/Select the Evidence" field.

Quality Assessment Strategy

The quality of the individual studies was assessed by one reviewer and independently checked for agreement by a second reviewer. Any disagreements were resolved by consensus and, if necessary, a third reviewer was consulted. The quality of the RCTs was assessed using standard checklists which were adapted to incorporate topic-specific quality issues (see Appendix 10.5 of the Assessment Report [see the "Availability of Companion Documents" field]).

Data Analysis

Studies were analysed within the following categories: otherwise healthy adults, 'at risk', elderly, children. Analyses of all trials, including those with mixed populations where data could not be subdivided according to the above categories, were also undertaken. Analyses were carried out for both the ITT (intention to treat; representative of the entire population recruited in the trials) and ITTI (intention to treat, confirmed, influenza positive) populations wherever possible.

Odd ratios (OR) and 95% confidence intervals (CI) were calculated for dichotomous outcomes. For continuous outcomes (time to event data), median differences and 95% CI were calculated. Where standard errors (SEs) were not available in publications or supplied by the companies for each arm of the trial, SEs around the medians were estimated from CI using the delta method, or from standard deviations (SD). Where a SE, SD, or a CI were not provided, SEs were calculated using percentiles extrapolated from Kaplan-Meier graphs wherever possible, using the method reported by Collett.

Median differences and 95% CI were pooled to produce a weighted median difference (WMD). A random effects model was used, unless there were four or fewer studies included in the analysis, in which case a fixed effect model was used, as the estimate of the heterogeneity parameter is likely to be unreliable with small numbers of trials. All meta-analyses were conducted in RevMan 4.2.9 (Cochrane Collaboration). The impact of using the number of patients randomised (N) in the analyses of continuous outcomes rather than the number with alleviated symptoms (r) (as used in the previous review by Turner) was assessed by re-analysing the data from the previous review using N, and comparing these to the original results where 'r' was used.

Heterogeneity was assessed using the Chi^2 test and I^2 statistic. Where the results of the tests for heterogeneity were statistically significant ($p<0.1$), the potential sources of the heterogeneity, such as patient population, different durations of symptoms prior to treatment, vaccination status, and quality criteria, were identified. For the binary outcomes sensitivity analyses were conducted to explore

the impact of the extent of loss to follow-up, where the overall drop-out rate was 10% or more. This could not be investigated for the continuous outcomes, as these were reported as medians, and individual patient data were unavailable for most trials.

As there were no direct head-to-head studies comparing zanamivir with oseltamivir that provided data for the outcomes being evaluated, an indirect comparison was undertaken using placebo as the common comparator, enabling indirect evidence to be utilized.

Cost-Effectiveness

Methods

The quality of included studies was assessed according to a general checklist based on that developed by Drummond together with a more specific checklist for decision-models from Philips. This information is summarised within the text of the report, alongside a detailed critique of each study and the relevance to the UK NHS. The differences in approaches and assumptions are then explored in detail in order to explain any discrepancies in findings and to identify key areas of remaining uncertainty. The findings from the review provide the basis for the development of a new model reported in Section 6 of the Assessment Report (see the "Availability of Companion Documents" field).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Manufacturer's Model

The current submission from the manufacturer of oseltamivir (Roche Products) included a decision-tree economic model that estimated the cost effectiveness of oseltamivir compared with zanamivir and usual care for the treatment of influenza, using separate pairwise comparisons. The model considered the following population subgroups separately: otherwise healthy adults; 'at-risk' adults (including older adults); otherwise healthy children aged 1 to 12 years; and otherwise healthy children aged 1 to 5 years.

The comparison of oseltamivir with usual care for the treatment of influenza produced base-case incremental cost-effectiveness ratios (ICERs) of 5452 pounds sterling per quality-adjusted life-year (QALY) gained for healthy adults, 5992 pounds sterling per QALY gained for healthy children aged between 1 and 12

years, 4687 pounds sterling per QALY gained for healthy children aged between 1 and 5 years and 652 pounds sterling for 'at-risk' adults. For all populations, zanamivir was dominated by oseltamivir (that is, oseltamivir was less costly and more effective than zanamivir).

Assessment Group Model

The Assessment Group conducted an independent economic assessment. The model was used to develop incremental estimates of the cost effectiveness of oseltamivir and zanamivir for the treatment of influenza compared with usual care without antiviral treatment.

Cost-effectiveness estimates for influenza treatment were presented for the following population groups: otherwise healthy children (aged 1 to 14 years); 'at-risk' children (aged 1 to 14 years); otherwise healthy adults (aged 15 to 64 years); 'at-risk' adults (aged 15 to 64 years) and the 'elderly' (defined as adults older than 65 years).

In base-case results, for each population the ICER for both oseltamivir and zanamivir (relative to usual care) was less than 20,000 pounds sterling per QALY gained, and across the separate populations ranged from 562 pounds sterling to 7035 pounds sterling per QALY gained. In healthy children and healthy adults oseltamivir dominated zanamivir, with ICERs of 7035 pounds sterling and 5521 pounds sterling per QALY gained, respectively. In 'at-risk' children, 'at-risk' adults and older people zanamivir extendedly dominated oseltamivir (that is, the ICER for oseltamivir treatment is higher than that of zanamivir and usual care and is therefore ruled out on the basis of extended dominance). The ICERs were 1752 pounds sterling per QALY gained for 'at-risk' children, 2270 pounds sterling for 'at-risk' adults and 562 pounds sterling for older people.

Consideration of the Evidence

The Committee considered the cost-effectiveness estimates for oseltamivir and zanamivir treatment in otherwise healthy populations. It considered that the most plausible presented ICERs in this group were from the scenarios exploring the combined effect of excluding hospitalisation and mortality benefits, increased general practitioner (GP) consultation rates with a subsequent reduction in the probability that an influenza-like illness is true influenza and a reduced decrement in quality of life of 0.2. The point estimate ICERs resulting from these scenarios ranged from 21,000 pounds sterling to 31,500 pounds sterling per QALY gained in healthy children and from 39,900 pounds sterling to 65,600 pounds sterling per QALY gained for healthy adults. The Committee considered that the ICERs of 21,000 pounds sterling to 31,500 pounds sterling per QALY gained in healthy children were underestimates of the true ICERs within the preferred set of assumptions accepted by the Committee. The Committee was also aware that the ICERs presented assumed treatment with oseltamivir in all cases, because oseltamivir dominated zanamivir in healthy populations. The Committee was mindful that if both oseltamivir and zanamivir were recommended, then the true ICERs for healthy populations would be higher. Therefore, the Committee concluded that oseltamivir and zanamivir for the treatment of influenza in otherwise healthy children and adults would not be a cost-effective use of National Health Service (NHS) resources.

The Committee further considered the cost-effectiveness estimates of oseltamivir and zanamivir in 'at-risk' populations. Having reviewed a number of the key parameters from the economic models, the Committee concluded that for 'at-risk' populations the economic estimates submitted by the Assessment Group and the manufacturer of oseltamivir were plausible. The Committee concluded that because the base-case estimates were all less than 20,000 pounds sterling per QALY gained for these population subgroups, then oseltamivir and zanamivir, within their licensed indications, could be recommended as cost-effective uses of NHS resources.

See Sections 4.2 and 4.3 of the original guideline document for a detailed discussion of the cost-effectiveness analysis.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Institute for Health and Clinical Excellence*: This guidance replaces 'NICE technology appraisal guidance 58' issued in February 2003. The review and re-appraisal of amantadine, oseltamivir and zanamivir for the treatment of influenza has resulted in a change in the guidance. Specifically*:

- *Â People with chronic neurological conditions and people with chronic liver disease are now considered 'at risk'.*
- *Zanamivir is now recommended as a treatment option for children between the ages of 5 and 12 years in 'at-risk' groups if influenza is circulating, and they can start treatment within 36 hours of first symptoms.*
- *Oseltamivir and zanamivir are now recommended as treatment options for 'at-risk' people in long-term and residential nursing homes during localised outbreaks (when influenza is not circulating), if there is a high level of certainty that the causative agent is influenza*.

This guidance has been prepared in the expectation that vaccination against influenza is undertaken in accordance with national guidelines. Vaccination has been established as the first-line intervention to prevent influenza and its complications, and the drugs described in this guidance should not in any way detract from efforts to ensure that all eligible people receive vaccination.

This guidance does not cover the circumstances of a pandemic, impending pandemic or a widespread epidemic of a new strain of influenza to which there is little or no community resistance.

Guidance

Oseltamivir and zanamivir are recommended, within their marketing authorisations, for the treatment of influenza in adults and children if **all** the following circumstances apply:

- National surveillance schemes indicate that influenza virus A or B is circulating*
- The person is in an 'at-risk' group as defined below
- The person presents with an influenza-like illness and can start treatment within 48 hours (or within 36 hours for zanamivir treatment in children) of the onset of symptoms as per licensed indications.

For the purpose of this guidance, people 'at risk' are defined as those who have one or more of the following:

- Chronic respiratory disease (including asthma and chronic obstructive pulmonary disease)
- Chronic heart disease
- Chronic renal disease
- Chronic liver disease
- Chronic neurological conditions
- Diabetes mellitus

People who are aged 65 years or older and people who might be immunosuppressed are also defined as 'at-risk' for the purpose of this guidance.

The choice of either oseltamivir or zanamivir in the circumstances described above should be made after consultation between the healthcare professional, the patient and carers. The decision should take into account the patient's preferences regarding drug delivery and potential adverse effects and contraindications. If all other considerations are equal, the drug with the lowest acquisition cost should be offered.

During localised outbreaks of influenza-like illness (outside the periods when national surveillance indicates that influenza virus is circulating in the community), oseltamivir and zanamivir may be offered for the treatment of influenza in 'at-risk' people who live in long-term residential or nursing homes. However, these treatments should be offered only if there is a high level of certainty that the causative agent in a localised outbreak is influenza (usually based on virological evidence of influenza infection in the initial case).

Amantadine is not recommended for the treatment of influenza.

*The Health Protection Agency in England (and the equivalent bodies in Wales and Northern Ireland) uses information from a range of clinical, virological and epidemiological influenza surveillance schemes to identify periods when there is a substantial likelihood that people presenting with an influenza-like illness are infected with influenza virus.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of zanamivir and oseltamivir in "at risk" children and adults with influenza

POTENTIAL HARMS

Zanamivir

Adverse effects associated with zanamivir are rare. They include bronchospasm and allergic phenomena.

Oseltamivir

Adverse effects associated with oseltamivir include gastrointestinal symptoms, bronchitis and cough, dizziness and fatigue and neurological symptoms such as headache, insomnia and vertigo. Skin rashes and allergic reactions and, rarely, disorders of the hepatobiliary system have been reported. Convulsions and neuropsychiatric disorders, mainly in children and adolescents, have also been reported but a causal link has not been established.

For full details of side effects and contraindications, see the Summary of Product Characteristics, available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance represents the view of the National Institute for Health and Clinical Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully

into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organizations in meeting core and developmental standards set by the Department of Health in "Standards for better health" issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by the National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- "Healthcare Standards for Wales" was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires local health boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- NICE has developed tools to help organisations implement this guidance (listed below). These are available on the NICE website (www.nice.org.uk/TA168) (see also the "Availability of Companion Documents" field).
    - A costing statement explaining the resource impact of this guidance
    - Audit support for monitoring local practice

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Amantadine, oseltamivir and zanamivir for the treatment of influenza. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Feb. 40 p. (Technology appraisal guidance; no. 168).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Feb (revised 2009 Feb)

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Dr Jane Adam, Radiologist, St George's Hospital, London; Professor AE Ades, Professor of Public Health Science, Department of Community

Based Medicine, University of Bristol; Dr Amanda Adler, Consultant Physician, Cambridge University Hospitals Trust; Dr Tom Aslan, General Practitioner, London; Professor David Barnett (*Chair*), Professor of Clinical Pharmacology, Leicester Royal Infirmary; Mrs Elizabeth Brain, Lay member; Dr Matt Bradley, Head of HTA and Business Development, Sanofi-aventis UK; Dr Robin Carlisle, Deputy Director of Public Health, Rotherham Primary Care Trust; Dr Karl Claxton, Professor of Health Economics, Department of Economics and Related Research, University of York; Dr Simon Dixon, Reader in Health Economics, University of Sheffield; Mrs Fiona Duncan, Clinical Nurse Specialist, Anaesthetic Department, Blackpool Victoria Hospital, Blackpool; Dr Paul Ewings, Statistician, Taunton and Somerset NHS Trust, Taunton; Professor John Geddes, Professor of Epidemiological Psychiatry, University of Oxford; Mr John Goulston, Chief Executive, Barking, Havering and Redbridge Hospitals NHS Trust; Mr Adrian Griffin, VP Strategic Affairs, LifeScan, Johnson and Johnson; Dr Richard Harling, Director of Public Health, Worcestershire Primary Care Trust and Worcestershire County Council; Professor Philip Home (*Vice-Chair*), Professor of Diabetes Medicine, Newcastle University; Dr Terry John, General Practitioner, London; Dr Vincent Kirkbride, Consultant Neonatologist, Regional Neonatal Intensive Care Unit, Sheffield; Dr Simon Maxwell, Senior Lecturer in Clinical Pharmacology and Honorary Consultant Physician, Queen's Medical Research Institute, University of Edinburgh; Dr Alec Miners, Lecturer in Health Economics, London School of Hygiene and Tropical Medicine; Dr Ann Richardson, Lay member; Mrs Angela Schofield, Chairman, Bournemouth and Poole Teaching Primary Care Trust; Mr Mike Spencer, General Manager, Facilities and Clinical Support Services, Cardiff and Vale NHS Trust; Dr William Turner, Consultant Urologist, Addenbrooke's Hospital, Cambridge University Hospitals NHS Trust; Dr Simon Thomas, Consultant Physician and Reader in Therapeutics, Newcastle Hospitals NHS Foundation Trust and Newcastle University; Mr David Thomson, Lay member; Dr Luke Twelves, General Practitioner, Cambridgeshire; Dr Norman Vetter, Reader, Department of Primary Care and Public Health, School of Medicine, University of Cardiff; Dr Paul Watson, Director of Commissioning, East of England Strategic Health Authority

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: National Institute for Clinical Excellence (NICE). Guidance on the use of zanamivir, oseltamivir and amantadine for the treatment of influenza. London (UK): National Institute for Clinical Excellence (NICE); 2003 Feb. 30 p. (Technology appraisal guidance; no. 58).

The review date for this guideline is November 2013.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Amantadine, oseltamivir and zanamivir for the treatment of influenza. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Feb. 2 p. (Technology appraisal 168). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Amantadine, oseltamivir and zanamivir for the treatment of influenza. Costing statement. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Feb. 2 p. (Technology appraisal 168). Available in Portable Document Format (PDF) from the NICE Web site.
- Amantadine, oseltamivir, and zanamivir for the treatment of influenza. Audit support. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009. 7 p. (Technology appraisal 168). Available in Portable Document Format (PDF) from the NICE Web site.
- Antiviral drugs for the treatment of influenza:Â a systematic review and economic evaluation. Assessment report. 2008. 340 p. Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1804. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Oseltamivir, zanamivir and amantadine for the treatment of influenza. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Feb. 4 p. (Technology appraisal 168).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the Department of Health Publications Order Line 0870 1555 455. ref: N1805. 11 Strand, London, WC2N 5HR.

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This NGC summary was completed by ECRI on August 2, 2006. This summary was updated by ECRI on November 21, 2006 following the FDA advisory on Tamiflu. This summary was updated by ECRI Institute on March 10, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Tamiflu (oseltamivir phosphate). This summary was updated by ECRI Institute on April 9, 2008 following the U.S. Food and Drug Administration (FDA) advisory on Relenza (zanamivir). This summary was updated by ECRI Institute on October 4, 2009.

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Date Modified: 3/1/2010